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Late-Onset Systemic Lupus Erythematosus With Lupus Nephritis in a 74-Year-Old Male: A Brief Case and Review

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Abstract

Rationale: Late-onset systemic lupus erythematosus (SLE) represents a specific subgroup of SLE, and although there is no strict age cut-off, 50 years is commonly used as the minimum age for disease onset. In this report, we present a case of a 74-year-old male with late-onset SLE and biopsy-proven lupus nephritis (LN).

Presenting concerns of the patient: A 74-year-old male was referred to the nephrology clinic with a rapidly rising creatinine from a baseline of 60 µmol/L to 176 µmol/L. His labs showed pancytopenia, a positive antinuclear antibodies (ANA), and hypocomplementemia.

Diagnoses: Renal biopsy showed focal proliferative glomerulonephritis that was immune-mediated and immunofluorescence showed C3, IgM, IgA, IgG, lambda, and C1q diffuse mesangial and glomerular basement membrane staining. Together these findings were in keeping with a diagnosis of stage III LN.

Interventions: Treatment included hemodialysis and induction with pulse methylprednisone and cyclophosphamide. He was then placed on the Euro-Lupus Protocol.

Outcomes: One year after the diagnosis, he was off dialysis, had no signs of fluid retention or uremia, and his creatinine had stabilized at ~ 330 µmol/L.

Lessons learned: To the best of our knowledge, this case represents the oldest known biopsy-confirmed case of late-onset SLE and LN. Late-onset SLE is uncommon and often overlooked as classical symptoms such as malar rash or photosensitivity may not be present. The American College of Rheumatology (ACR) guidelines for treatment of LN can be applied to these patients but physicians should be cognizant of the fact that these patients may not tolerate immunosuppressive therapy as well as younger patients.

Abrégé

Contexte: La forme tardive du lupus érythémateux disséminé (LED) constitue un sous-groupe particulier de la maladie. Bien qu'il n'existe pas de limite d'âge précise pour établir la manifestation tardive du LED, cette limite est généralement fixée à 50 ans. Dans ce rapport, nous présentons le cas d'un patient âgé de 74 ans atteint de la forme tardive du LED et d'une néphropathie lupique (NL) avérée par biopsie.

Présentation du cas: Il s'agit d'un patient âgé de 74 ans orienté en clinique de néphrologie en raison d'une augmentation rapide de son taux de créatinine, lequel était passé de 60 µmol/L (valeur initiale) à 176 µmol/L. Les analyses de laboratoire ont confirmé la présence d'une pancytopénie, d'une hypocomplémentémie et d'un résultat positif pour la détection des anticorps antinucléaires (AAN).

Diagnostic: La biopsie rénale a révélé la présence d'une néphrite de Löhlein à médiation immunologique et l'immunofluorescence a mis en évidence une coloration diffuse des membranes basales mésangiales et glomérulaires pour les fragments de C3 et de C1q, pour les IgM, les IgA, les IgG, de même que pour les chaînes Lambda. Ces constatations mises ensemble concordaient avec un diagnostic de NL de stade 3.

Intervention: Le patient a été traité par hémodialyse et par l'administration intermittente de méthylprednisone et de cyclophosphamide. Il a par la suite suivi le protocole « Euro-Lupus ».

Résultats: Un an après le diagnostic, le patient n'était plus sous dialyse, ne montrait aucun signe d'urémie ou de rétention hydrique, et son taux de créatinine était stable autour de 330 µmol/L.

Enseignements tirés: À notre connaissance, ce patient représente le cas connu le plus tardif de manifestation d'un LED et d'une NL confirmée par biopsie. La forme tardive du LED est plutôt rare et souvent négligée en raison de l'absence d'érythème malaire ou de réaction de photosensibilité; des symptômes normalement associés à la maladie. Les recommandations de l'ACR pour le traitement de la NL peuvent être appliquées chez ces patients, mais les médecins doivent garder à l'esprit que ces patients pourraient ne pas tolérer les traitements immunosuppresseurs aussi bien que les patients plus jeunes.

Keywords
SLE (systemic lupus erythematosus), glomerulonephritis, complement-mediated glomerulonephritis, AKI (acute kidney injury)

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What was known before

Late-onset systemic lupus erythematosus (SLE) represents a specific subgroup of SLE and is often initially missed leading to a significant delay in diagnosis.

What this adds

The key take-home points from this report are the following: (1) Consider the diagnosis of late-onset SLE and LN in elderly patients with renal failure; (2) be aware that late-onset patients do not present with typical SLE symptoms and serology/renal biopsy should be used when available in conjunction with the history; and (3) these patients have lower rates of renal failure/nephritis. However, if they present with nephritis, they should be treated with immunosuppression as tolerated.

Introduction

Elderly patients frequently present to hospital with nonspecific symptoms such as fatigue, weight loss, and acute kidney injury. In this report, we present a 74-year-old male with late-onset systemic lupus erythematosus (SLE) and lupus nephritis (LN) to highlight commonly associated symptoms and serological markers to aid other physicians in the early diagnosis of this condition.

Presenting Concerns

A 74-year-old male presented to clinic with a rapidly rising creatinine from a baseline of 60 µmol/L to 176 µmol/L within 3 months. The patient had generalized fatigue, fevers, night sweats, and had lost 15 lbs. His past medical history was significant for coronary artery disease with bypass surgery, hypertension, and type 2 diabetes.

Clinical Findings

He had a blood pressure of 140/77, heart rate of 107, and a temperature of 36.9°C. His physical examination was unremarkable except for a livedo reticularis–like rash across his chest and a nonblanchable, nonpruritic rash across his back. He had no dry skin, dry eyes, conjunctiva changes, or musculoskeletal weakness/pain. His labs showed pancytopenia, a positive antinuclear antibodies (ANA) (1:160), and decreased C3/C4 at 0.18 g/L and 0.03 g/L, respectively. Serology was positive for anti-La antibody, negative for anti-dsDNA, ANCA, anti-GBM, anti-cardiolipin antibody, and rheumatoid factor (RF). Serum and urine electrophoresis was negative. Microscopy showed heme-granular casts and his albumin to creatinine ratio was 305. He had no history of oral/mucosal changes, photosensitivity, skin rashes, or arthritis/joint pains.

Diagnostic Assessment

Renal biopsy showed a focal proliferative glomerulonephritis that was immune-mediated. Three of 43 glomeruli were globally sclerotic and 2 glomeruli contained cellular crescents. There was mild interstitial fibrosis and tubular atrophy. The majority of glomeruli showed mesangial hypercellularity. Four glomeruli were examined by direct immunofluorescence, which showed the following: C3 diffuse intense granular mesangial and glomerular basement membrane staining; IgM, IgA and C1q diffuse moderate granular mesangial and glomerular basement membrane staining; IgG and lambda diffuse light granular mesangial and glomerular basement membrane staining. Kappa and fibrinogen showed no significant staining. These findings were in keeping with a diagnosis of stage III lupus nephritis (LN). A skin biopsy from the back showed no indication of lichenoid infiltrate or a lupus reaction.

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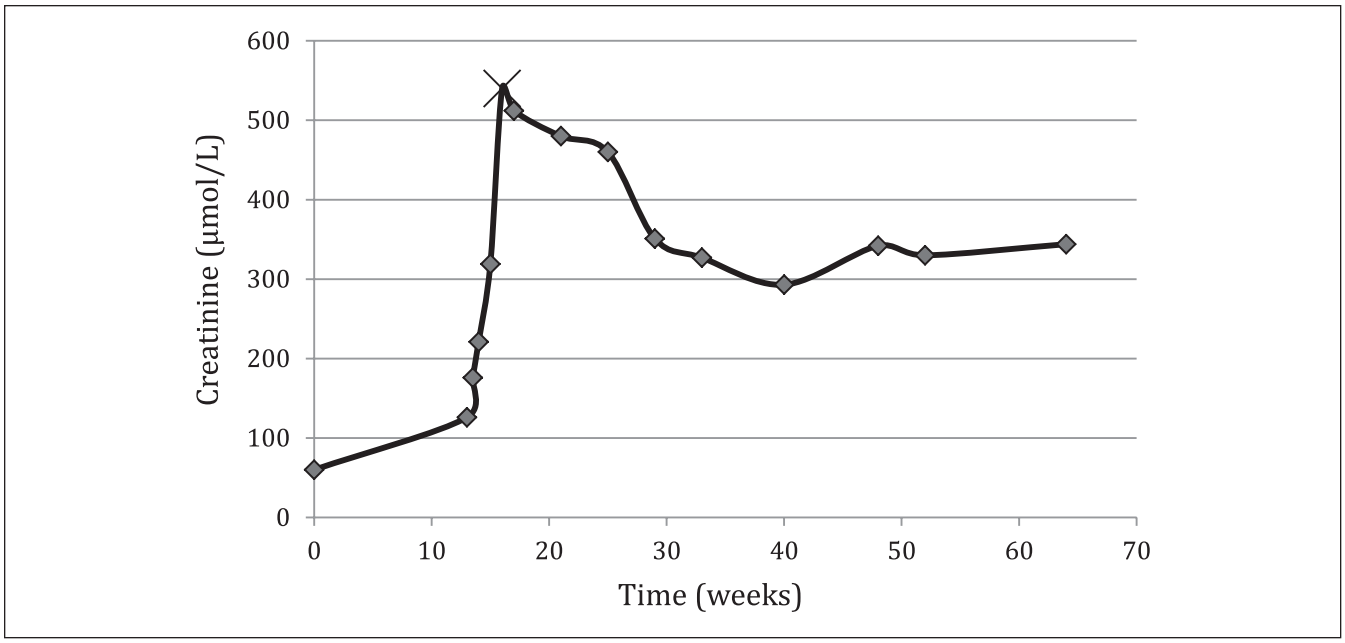

Figure 1. Change in patient's creatinine over time (weeks). X denotes initiation of hemodialysis and immunosuppression.

Therapeutic Focus and Follow-up

The patient's creatinine rose to 560 μmol/L within 72 hours. He was started on hemodialysis and treated with pulse methylprednisone and cyclophosphamide. His rash disappeared after induction therapy and he was started on the Euro-Lupus Protocol. His prednisone was tapered to 7 mg daily (over ~ 6 months) and azathioprine was started for maintenance therapy (mycophenolate mofetil was tried but the patient was not able to tolerate the gastrointestinal side effects). After 6 months, he was able to come off dialysis; his C3/C4 increased to 0.62 g/L and 0.12 g/L, respectively; and his pancytopenia resolved. One year after diagnosis, his creatinine stabilized at ~ 330 μmol/L. The change in his renal function from baseline has been shown in Figure 1.

Methodology

Patient consent was obtained prior to publication and a literature search was conducted through Medline and PubMed. In brief, the Medline database was searched for "late-onset lupus" and restricted to human studies. This yielded 21 publications, which were screened for relevance. Relevant studies were read in full and their references were screened. This process was repeated in PubMed (initial search yielded 147 results).

Discussion

SLE is a chronic multisystem disorder most commonly affecting young women[1,2] and approximately 35% of those diagnosed with SLE will have some evidence of LN at the time of diagnosis.[3,4] The optimal criterion for diagnosis is a renal biopsy with histopathology demonstrating immune complex–mediated glomerulonephritis compatible with LN.[3,5]

The patient in our case demonstrated late-onset SLE with LN. Late-onset SLE represents a specific subgroup of SLE, and although there is no strict age cutoff, 50 years is commonly used as the minimum age of disease onset.[6,7] As with adult-onset SLE, the incidence is higher in females with a female to male ratio ranging between 1-7:1,[1,2,6,8] although there have been sparse case report data showing males with late-onset SLE and LN.[2,9,10] The patient in our case was a 74-year-old male with SLE and biopsy-proven LN, but lacked the multisystem presentation often associated with SLE. Based on the literature, late-onset SLE is generally more benign, with a lower rate of renal complications.[6,7]

A pooled analysis by Boddaert et al across over 700 cases showed that patients with late-onset SLE have a more benign disease onset leading to a delay in diagnosis.[7] This refers primarily to a decreased incidence of nephritis and a different constellation of symptoms (see Table 1). Delay in diagnosis is often due to the decreased prevalence of common disease markers such as photosensitivity or malar rash and attributing symptoms to other comorbid conditions commonly seen in elderly patients.[6,7,11] As a result, the time from symptom onset to diagnosis has been reported as being as high as 60 months for late-onset SLE compared with 19 to 24 months for adult-onset SLE.[6,7,12] Some studies have also shown that late-onset SLE patients have an increased prevalence of serositis, pulmonary involvement, positive RF, hypocomplementemia, and anti-Ro/anti-La antibodies. These patients

Table 1. Common Clinical and Serology Markers That Are Increased or Decreased in Late-Onset Systemic Lupus Erythematosus.

Clinical	Decreased female/male ratio
	Decreased malar rash
	Decreased nephritis
	Increased serositis
	Increased pulmonary involvement
	Increased overlap with Sjögrens syndrome
Serology	Increased rheumatoid factor positivity
	Increased anti-Ro/La antibodies

also have a higher incidence of Sjögrens syndrome, which often coexist with SLE, although the exact rationale for this has not been clarified.[6,7,11,13]

A comparative analysis of SLE patients showed that those >65 years had a higher incidence of positive anti-dsDNA during follow-up, but not at the time of diagnosis (but no difference in disease activity).[12] With respect to anti-dsDNA antibodies, studies have shown mixed results. Sassi et al noted decreased anti-dsDNA antibody levels in late-onset SLE patients.[14] This trend was also seen in a comparative study across 200 Korean patients.[11] However, an older analysis of Brazilian patients found slightly higher anti-dsDNA levels in late-onset SLE.[15] These data suggest that the value of anti-dsDNA in late-onset SLE is unclear and recent data suggest that anti-dsDNA antibodies may not be the most specific biomarker for SLE.[16]

Patients with late-onset SLE have a higher incidence of elevated creatinine and a decreased creatinine clearance (CrCl) at presentation, compared with adult-onset SLE.[17] Late-onset SLE patients had an average CrCl of 49.1 mL/min, compared with 71.2 mL/min for adult-onset patients.[17] Late-onset SLE patients were also more likely to have hypertension at disease onset. This combined with the natural loss of renal function with age may explain the higher creatinine at the time of diagnosis. However, these differences in baseline renal function did not correlate with new renal damage, rates of remission, or renal recovery.[17,18] Furthermore, nephritis and nephropathy were less likely in late-onset SLE.[7,11,14,19] A study of 598 SLE patients showed the rates of nephritis to be 26.6% in the late-onset group compared with 39.8% in the adult-onset group.[14] In addition, a pooled analysis of cases in the literature has similarly shown the rates of nephritis to be 28.6% and 42.7%, respectively.[7]

Finally, late-onset SLE patients were more likely to die due to treatment-related complications such as sepsis and had an increased incidence of fever.[7,12,13] Age >50 years, male gender, and low C3 levels may be linked to an increased risk of death due to SLE.[18] In terms of management, late-onset patients are treated according to the American College of Rheumatology (ACR) guidelines for SLE.[3] However, they do not require immunosuppression as frequently due to lower rates of nephritis (a common reason to require immunosuppression). Five-year survival rates for late-onset SLE are between 72% and 84% compared with ~90% to 95% for younger-onset patients. However, there is no clear indication that this difference is due to disease activity/complications.[7,12,13,20] Although late-onset SLE does not independently increase mortality, the increased mortality noted in this group has been explained by the presence of increased comorbidities at disease onset, most notably, hypertension, altered immune function, and decreased tolerance to immunosuppressive therapy.[8,12,17,18]

Summary

To the best of our knowledge, this case represents the oldest known biopsy-confirmed case of LN. The severity of renal disease in this case was somewhat atypical for late-onset SLE and suggests that more research is required to identify and characterize this disease. Although the incidence of late-onset SLE is uncommon, it represents a unique subtype of SLE and should be treated accordingly. The ACR guidelines for treatment of LN can be applied to these patients but physicians should be cognizant of the fact that they may not tolerate immunosuppressive therapy as well as younger patients.

Ethics Approval and Consent to Participate

Written patient consent and approval was obtained prior to publication.

Consent for Publication

All authors consent for publication.

Availability of Data and Materials

Not applicable.

Declaration of Conflicting Interests

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